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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/869,877	07/06/2001	Palle Schneider	10179.204-US	4404

25908 7590 08/12/2003

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EXAMINER

SLOBODYANSKY, ELIZABETH

ART UNIT PAPER NUMBER

1652

DATE MAILED: 08/12/2003

12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/869,877

Applicant(s)

SCHNEIDER ET AL.

Examiner

Elizabeth Slobodyansky

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 May 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 16-45 is/are pending in the application.
- 4a) Of the above claim(s) 17-34, 37, 38 and 43-45 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 16, 35, 36 and 39-42 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: alignment SEQ ID NOs: 1 & 10.

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DETAILED ACTION

The amendment filed May 16, 2003 canceling claims 1-15 and adding claims 16-45 has been entered.

Claims 16-45 are pending.

Election/Restriction

Newly submitted claims 43-45 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: claims 43-45 are drawn to methods of use of a variant of claim 16. A variant of claim 16 and methods of use thereof are known in the prior art and therefore, there is no special technical feature linking a variant laccase and methods of use thereof that as a whole makes a contribution over the prior art (WO 98/38286).

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 17-38, drawn to non-elected species and claims 43-45, drawn to methods of use of a variant, are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 40-42, drawn to a detergent composition comprising a variant laccase of claim 16, are rejoined with claim 16.

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In view of the applied prior art, claims 35 and 36 are examined together with claim 16.

Thus, claims 16, 35, 36, 39 and 40-42 are under examination. Claims 17-34, 37, 38 and 43-45 are withdrawn.

Specification

The examiner notes that the sequence search performed at US PTO shows that SEQ ID NO:10 is about 22 % identical to SEQ ID NO:1 whereas the specification states 56.5% identity (page 2, lines 30-31). A copy of US PTO search result is attached hereto. Clarification is required.

Claim Objections

Claim 36 is objected to because of the improper recitation of Markush group (MPEP 2173.05(h)). Further, "A" should be deleted. Appropriate correction is required.

Claim 39 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 39 depends from claim 16. Claim 16 is drawn to a *Myceliophthora thermophila* laccase variant with a mutation at position corresponding to a position in SEQ ID NO:10. Claim 39 recites the

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limitation "wherein *Myceliophthora thermophila* laccase has an amino acid sequence of SEQ ID NO:10". SEQ ID NO:10 is the amino acid sequence of *Myceliophthora thermophila* laccase.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 16, with dependent claims 35, 36 and 39-42, is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 16 is directed to a variant of a *Myceliophthora thermophila* laccase which comprises a mutation corresponding to at least one of the 11 specific positions in SEQ ID NO:10. Since "comprising" is open language, the number of allowed additional mutations is not limited. The specific mutations represent about 0.17%-2.4% of SEQ ID NO:10 that is 573 amino acid long. This amounts to said genus of variants being characterized by laccase function. Therefore, the genus of said variant laccases encompasses enzymes with structures with any possibly low homology to SEQ ID

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NO:10 having different properties. While applicants disclose variants having the amino acid sequences that differ from SEQ ID NO:10 by mutations at the indicated positions, the claimed genus is highly variable as it encompasses great number of undisclosed variants with undisclosed structures and properties.

Moreover, the specification fails to describe any other representative species with changes in positions other than specifically indicated by any identifying characteristics or properties other than the "functionality" of being a laccase variant and fails to provide any structure: function correlation present in all members of the claimed genus. Therefore, the specification is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Claims 16, 35, 36 and 39-42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a variant of a *Myceliophthora thermophila* laccase having an amino acid sequence that differs from SEQ ID NO:10 by a mutation corresponding to at least one of the 11 specific positions therein, does not reasonably provide enablement for a variant of a *Myceliophthora thermophila* laccase having an amino acid sequence that comprises a mutation corresponding to at least one of the 11 specific positions wherein said variant amino acid sequence has

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unknown homology to SEQ ID NO:10. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, how to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) considered in determining whether undue experimentation is required, are summarized the predictability or unpredictability of the art, and (8) the breadth of the claims.

Claims 16 and 39 are directed to a variant of a *Myceliophthora thermophila* laccase having an amino acid sequence comprising a mutation in SEQ ID NO:10 corresponding to at least one of the 11 specific positions of any structure and properties (the number of possible mutations is not limited). Claims 35 and 36 are directed to a variant of a *Myceliophthora thermophila* laccase having an amino acid sequence comprising a specific mutation at position 506 in SEQ ID NO:10 of any structure and properties (the number of possible mutations is not limited).

Claims 16, 35, 36 and 39-42 are so broad as to encompass any variant of a *Myceliophthora thermophila* laccase having an amino acid sequence comprising a

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mutation corresponding to at least one of the 11 specific positions in SEQ ID NO:10 with unknown possible low homology to the laccase of *Myceliophthora thermophila*. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of variant laccase enzymes broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the amino acid sequence of the variants having the mutations at the specific positions in SEQ ID NO:10.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to

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modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass any mutant luciferase having the requisite property with an undisclosed homology to the laccase of *Myceliophthora thermophila* in which the amino acid corresponding to the specific positions in SEQ ID NO:10 is mutated because the specification does not establish: (A) regions of the protein structure which may be modified without effecting laccase activity; (B) the general tolerance of laccases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any laccase residues with an expectation of retaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of amino acid modifications in laccase of *Myceliophthora thermophila* sequence in addition to the specific mutations recited in the claim. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, making variant laccases is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

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Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 16, 35, 36 and 39-42 are rejected under 35 U.S.C. 102(b) as being anticipated by Svendsen et al.

Svendsen et al. (WO 98/38286, form PTO-1449) teach a variant of *Myceliophthora thermophila* laccase with substitution A506E (7, line 14; claim 4). They teach a detergent composition comprising thereof (claims 17-20).

Response to Arguments

With regard to the prior Danish applications, the US PTO is in the process of obtaining them from the International Bureau. Applicants will be informed when the applications are received.

Applicant's arguments filed May 16, 2003 have been fully considered but they are not persuasive.

Applicants argue with regard to the homology between SEQ ID NO:10 and SEQ ID NO:1 that "the specification is correct, they are 56.5% identical". There is

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disagreement between Applicants assertion and the PTO search results, *supra*, that requires clarification.

With regard to the written description rejection, Applicants argue that “the specification fully describes the laccase variants of the present invention. Based on Applicants’ disclosure, the skilled artisan would to be led to make other mutations in addition to the mutations recited in the claims to obtain the benefits described in the present application” (Remarks, page 6, 2nd paragraph). This is not persuasive because Applicants described the laccase variants that differ from SEQ ID NO:10 by mutations at the specific positions. However, the claims encompass variants of laccase having unknown homology to SEQ ID NO:10 comprising said mutations. As explained above, there is no limitation on the structure of a laccase variant except for the recited positions.

With regard to the enablement rejection, Applicants argue that “the specification describes laccases modified at specific positions. In addition, the specification provides that the variants can be modified at other positions and includes examples of such other positions. Based on Applicants’ disclosure, the skilled artisan would be able to make laccase variants that are modified at the recited positions as well as other positions” (paragraph bridging pages 6 and 7). This is not persuasive because the claims are not drawn to variants that are modified at the recited positions as well as

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"other positions". Said "other positions" are not recited in the claims. Therefore, claims are drawn to variants of laccase having unknown homology to SEQ ID NO:10.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky whose telephone number is (703) 306-3222. The examiner can normally be reached Monday through Friday from 9:30 AM to 6:00 PM.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX phone number for Technology Center 1600 is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Center receptionist whose telephone number is (703) 308-0196.

A handwritten signature in cursive script that reads "E. Slobodyansky". The signature is written in black ink and is positioned above the printed name and title.

Elizabeth Slobodyansky, PhD
Primary Examiner

August 7, 2003

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10. US-09869877-lvs10 (1-539)

US-09869877-10 Sequence 10: Application US/09869877

Initial Score = 136 Optimized Score = 290 Significance = -0.94
 Residue Identity = 22% Matches = 126 Mismatches = 375
 Gaps = 24 Conservative Substitutions = 37